UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

NOVARTIS AG, NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiffs, v. NOVADOZ PHARMACEUTICALS LLC, MSN PHARMACEUTICALS INC., MSN LABORATORIES PRIVATE LIMITED, Defendants.	No. 25-CV-00849-EP-JRA

DECLARATION OF MARTIN SHIMER IN OPPOSITION

TO PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTIVE RELIEF

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I. PROFESSIONAL BACKGROUND

1. I received a Bachelor of Science in Pharmacy from the University of Maryland at Baltimore in 1993. I received a Certificate in Public Health from Georgetown University in 2009. I received the Certificate in Public Health while I was employed by the United States Food & Drug Administration ("FDA").

2. In July 2000, I was Commissioned as an Officer in the United States Public Health Service and accepted an assignment with FDA's Office of Generic Drugs ("OGD").[1] While serving in OGD, I served in multiple positions until my retirement in July 2022.

3. From July 2000 through August 2003, I worked as a Consumer Safety Officer in the Regulatory Support Branch of OGD. During this period, I reviewed newly submitted Abbreviated New Drug Applications ("ANDAs") to determine whether the applications were satisfactory and satisfied the requirements for filing acceptance and technical discipline review.

4. In August 2003, I was promoted to Branch Chief of the Regulatory Support Branch. I spent ten years in this role and supervised a team of roughly 8 to 16 individuals with responsibility for performing ANDA filing reviews. During this time, I developed expertise in the legal requirements for ANDA sponsors. In 2005, I

1 *Office of Generic Drugs*, U.S. Food & Drug Admin, https://www.fda.gov/about-fda/cder-offices-and-divisions/office-generic-drugs (last visited Feb. 4, 2025).

assumed responsibility for reviewing ANDAs to ensure that all legal requirements were satisfied prior to FDA taking an approval action.

5. In April 2013, I was promoted to the Deputy Director of the Division of Labeling and Program Support. In that role, I assisted the Division Director with oversight of all project managers, labeling reviewers, the Regulatory Support Branch, and the Orange Book[2] staff. I served in this role for roughly 18 months from April 2013 until October 2014. During this time, I had direct oversight of the legal review for ANDA submissions.

6. During the 2013 to 2014 time period, OGD was reorganized. As part of this process, I was promoted to Deputy Director of the Division of Legal and Regulatory Support in October 2014, and I served in this role until my retirement on June 30, 2022. In this role, I was tasked with building and training the Patent and Exclusivity Team. As its name would suggest, this team was responsible for the same legal requirement review mentioned previously. However, it was also responsible for administering the provisions including exclusivity for Competitive Generic Therapies; administering, and granting prioritization of original and

2 The "Orange Book" is a publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" that identifies FDA-approved drugs and related patent and exclusivity information. *Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. Food & Drug. Admin., https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book (last visited Feb. 4, 2025).

supplemental ANDAs; and assisting with resolving drug shortages involving ANDAs.

7. During my 22 years at FDA, I also developed expertise in many areas related to regulation of ANDAs, their review, and the resolution of issues that impact ANDAs. More specifically, those areas included:

a. All aspects of the administration of the Orange Book;

b. Member of the Center for Drug Evaluation and Research ("CDER") Exclusivity Board from the board's inception until my retirement;

c. Coordinator of the President's Emergency Plan for AIDS Relief ("PEPFAR") for the OGD;

d. Contributor for Generic Drug User Fee Act ("GDUFA") I negotiations that ran from October 1, 2012 through September 30, 2017; and

e. Member of negotiating term for GDUFA II that ran from October 1, 2017, through September 30, 2022.

8. While at FDA, I was exposed to and gained experience dealing with a broad range of issues related to FDA policy, FDA practice, and regulatory compliance. I was also exposed to and gained experience addressing issues related to drug misbranding.

9. In July 2022, I joined Lachman Consultant Services, Inc. ("Lachman") as the Executive Director of Regulatory Services. At Lachman, I oversee the

members of the regulatory team, serve as a consultant to industry, and assist clients with any number of issues that may arise with respect to their applications. In my current role at Lachman, I regularly advise clients on issues related to FDA practice and regulatory compliance.

10. Based on my experience at the FDA and in the industry, I am intimately familiar with the regulatory steps, approvals and authorizations required before a company can commercially market a generic or authorized generic drug product, including the additional regulatory steps, approvals, and authorizations required ***after*** the FDA approves a company's ANDA.

11. I provide this declaration in opposition to the motion for a preliminary injunction brought by Plaintiffs Novartis AG and Novartis Pharmaceutical Corporation (collectively, "Novartis") against Defendants Novadoz Pharmaceuticals LLC, MSN Pharmaceuticals Inc., and MSN Laboratories Private Limited (collectively, "MSN").

12. Attached as **Exhibit A** is my curriculum vitae. It contains a description of my educational background, professional achievements, qualifications, publications.

13. A list of the prior expert testimony I have offered in the last five years is attached as **Exhibit B**.

14. My employer Lachman Consulting is being compensated at $750 per hour for my work on this case. My compensation is not contingent on the outcome of this litigation or upon any opinions that I may express.

15. I considered certain case-related documents in preparing this declaration. The specific information I have considered is cited in the footnotes of the text. Information not cited in the footnotes which I considered while developing this declaration are listed below:

16. Complaint, filed in *Novartis v. Novadoz Pharmaceuticals, LLC*, No. 25-CV-00849 (D.N.J. Jan. 30, 2025), ECF 1.

17. Memorandum of Law in Support of Novartis's Preliminary Injunction Motion filed in filed in *Novartis v. Novadoz Pharmaceuticals, LLC*, No. 25-CV-00849 (D.N.J. Jan. 31, 2025), ECF 4-1.

18. Declaration of Dr. Arash Nayeri filed in Support of Novartis's Preliminary Injunction Motion filed in *Novartis v. Novadoz Pharmaceuticals, LLC*, No. 25-CV-00849 (D.N.J. Jan. 31, 2025), ECF 4-11.

19. ANDA 213748 from MSN Laboratories Private Limited (Novadoz Pharmaceuticals LLC).

20. *Novartis Pharms. Corp. v. Becerra*, No. 24-CV-02234 (DLF), 2024 WL 4492072, at *1 (D.D.C. Oct. 15, 2024).

II. THE FDCA DRUG APPROVAL PROCESS

21. The Federal Food, Drug, and Cosmetic Act ("FDCA") requires that any drug product introduced into interstate commerce must be the subject of an approved application.[3] For new or "brand" drugs, the sponsor submits a New Drug Application ("NDA") to FDA for review and approval.[4] In this case, the "sponsor" is the pharmaceutical company seeking approval of the new drug.[5] Before an NDA is submitted, a sponsor spends many years conducting research and testing the product. This pre-submission process consists of discovery and preclinical testing and then phases I, II, and III of development.[6] In total, this process, can, on average, take at least 10 years.[7] Once completed, a sponsor is then able to submit the NDA to FDA for review.[8] If FDA determines that the drug is both safe and effective for

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3 21 U.S.C. § 355(b)(1), (j).

4 21 U.S.C. § 355(b)(1).

5 *New Drug Application (NDA)*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/types-applications/new-drug-application-nda#:~:text=The%20NDA%20application%20is%20the,become%20part%20of%20the%20NDA (last updated Jan. 21, 2022).

6 *The Drug Development Process*, U.S. Food & Drug Admin., https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process (last updated Jan. 4, 2018).

7 *See* Cong. Budget Off., Research and Development in the Pharmaceutical Industry 2 (April 2021), *available at* https://www.cbo.gov/publication/57126. Gaurav Agrawal, Felix Bader, Jan Gunther, and Stephan Wurzer, *Fast to first-in-human: Getting new medicines to patients more quickly*, McKinsey & Co. (Feb. 10, 2023), https://www.mckinsey.com/industries/life-sciences/our-insights/fast-to-first-in-human-getting-new-medicines-to-patients-more-quickly.

8 *The Drug Development Process*, *supra* note 6.

the intended use and patient population, the NDA will be approved, and the product can be legally marketed in the United States.[9] Brand drugs are often subject to periods of both regulatory exclusivity and, separately, patent protection.[10]

III. GENERIC DRUG APPROVAL PROCESS

22. Generic drugs are approved via an abbreviated process. The application required to legally market a generic drug product is referred to as an ANDA.[11] ANDAs rely upon the FDA's previous finding of safety and efficacy for an NDA and therefore are not required to undertake the same clinical development and trial process.[12] ANDA sponsors are required to establish that their drug product is both a pharmaceutical equivalent of and bioequivalent to a Reference Listed Drug ("RLD").[13]

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9 *Step 4: FDA Drug Review*, U.S. Food & Drug Admin., https://www.fda.gov/patients/drug-development-process/step-4-fda-drug-review.

10 *Frequently Asked Questions on Patents and Exclusivity*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity.

11 *See* 21 U.S.C. § 355(j); *Abbreviated New Drug Application (ANDA)*,U.S. Food & Drug Admin., https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-anda (last updated Dec. 16, 2022).

12 21 U.S.C. § 355(j)(2)(A)(i); 21 C.F.R. § 314.3(b) (defining "Reference listed drug"), § 314.94(a)(3).

13 21 U.S.C. § 355(j)(2)(A)(i)-(iv); 21 C.F.R. § 314.94(a)(4)-(7).

23. Pharmaceutical equivalence means that a drug contains identical amounts of the identical active ingredient, has the same dosage form, strength, route of administration, and conditions of use as an existing NDA.[14] Bioequivalence means that the ANDA product has established that its rate and extent of absorption of a drug is not significantly different to a Reference Listed Drugs when administered at the same dose.[15]

24. In order to establish bioequivalence, an ANDA sponsor must first formulate and develop its drug product and then conduct testing in subjects referred to as in-vivo testing.[16] The classic bioequivalence study is where a subject first receives a dose of the test product (the ANDA product for which approval is being sought). Samples of the subject's blood are then taken at pre-defined time intervals, and those samples are then analyzed for the content of the drug. This same subject then receives a dose of the RLD with the same intervals of sampling. These results are then compared statistically and if certain criteria are met the products are considered bioequivalent.

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14 *Orange Book Preface*, U.S. Food & Drug Admin, https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface#:~:text=Pharmaceutical%20equivalents%20are%20drug%20products,require%20a%20reservoir%20or%20overage (last updated Sept. 11, 2024).

15 *Id.*

16 *Id.*

25. Generally, bioequivalence testing is required for most solid oral dosage forms that act systemically in the human body.[17] FDA's regulations require that the most accurate, sensitive, and reproducible method for establishing bioequivalence be utilized by applicants.

26. To assist ANDA sponsors with developing ANDAs and provide FDA's current thinking on the most accurate, sensitive, and reproducible method for establishing bioequivalence, FDA generally publishes a specific type of guidance outlining the number and type of bioequivalence studies that ANDA sponsors should conduct to establish bioequivalence of their proposed product to a branded RLD. This guidance is referred to as Product Specific Guidance (PSG). FDA published the original version of the PSG for ENTRESTO® in April 2016 and updated the PSG in October 2024.[18]

IV. BENEFICIAL ASPECTS OF GENERIC DRUGS TO THE PUBLIC

27. In order to assure timely access to generic drugs, FDA published the Drug Competition Action Plan with the stated goal to "further encourage robust, timely market competition for generic drugs and help bring greater efficiency and transparency to the generic drug review process, without sacrificing the scientific

17 *Id.*

18 U.S. Food & Drug Admin., Draft Guidance on Sacubitril; Valsartan (2024).

rigor underlying our generic drug program."[19] Moreover, FDA communicated that the overall goal of the Plan was to "spur competition that improves consumer's access to the medicines they need."[20]

28. Even though FDA does not play a role in the setting of drug prices, FDA recognizes that robust competition in the pharmaceutical industry via availability of high-quality generic products enhances patient access to certain drug therapies due to the reduction in prices associated with multiple approved ANDAs that compete among themselves and with the branded RLD based on price.

29. FDA published a report in December 2019 titled "Generic Competition and Drug Prices: New Evidence Linking Greater Competition and Lower Generic Drug Prices."[21] This report analyzed the impact of the number of generic market entrants, where those entrants must first achieve FDA approval, greatly influences the price of drug products.[22] When a single generic competitor enters the market, a price reduction of approximately 39% than the branded price is realized but once six

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19 *FDA Drug Competition Action Plan*, U.S. Food & Drug Admin. https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan (last updated Jan. 15, 2025).

20 *Id.*

21 Ryan Conrad, Ph.D. & Randall Lutter, Ph.D., *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Genetic Drug Prices*, U.S. Food & Drug Admin. (Dec. 2019), https://www.fda.gov/media/133509/download.

22 *Id.* at 2.

or more generic competitors have entered the market price reduction of 95% in comparison to the branded price can be realized.[23] In part, FDA's analysis was based on data from the Center for Medicare and Medicaid Services (CMS), where the cost savings from generic competition are realized by the federal government in the form of reduced medication expenditures for beneficiaries.[24]

30. Novartis received approval for all three strengths of ENTRESTO® Tablets on July 7, 2015 and while FDA has approved 11 ANDAs for generic versions of ENTRESTO® between May 28, 2024 and present, none of these ANDAs have commenced marketing. Thus, Novartis has benefitted from almost 10 years of monopoly pricing for ENTRESTO® Tablets. It cannot be disputed that ENTRESTO® is both an effective therapy for patients and is expensive. ENTRESTO® was one of the first ten branded RLD products the Federal Government selected for mandatory price negotiations under the Inflation Reduction Act (IRA). Drugs may be subject to the IRA if they have been approved for at least 7 years and do not face any generic competition, both of these criteria apply to ENTRESTO®. Based on a November 1, 2023 Fact Sheet published by the Assistant Secretary for Planning and Evaluation (ASPE), approximately 521,000 enrollees in

23 *Id.* at 2–3.
24 *Id.* at 5.

Medicare Part D received ENTRESTO® therapy at a cost of approximately $2.5 billion.

31. To protect the "golden goose" that is ENTRESTO®, Novartis has engaged in multiple tactics to first convince FDA not to approve generics of ENTRESTO® unless ANDAs met certain conditions deemed critical by Novartis. Novartis submitted two Citizens Petitions to FDA, the first in 2019 broadly claiming that ANDAs needed to meet certain requirements for establishing sameness of the active ingredients sacubitril and valsartan, and then in 2022 Novartis submitted their second petition challenging the ability of ANDA applicants to remove language from their proposed labels, as permitted by section 505(j)(2)(A)(viii) of the Federal Food Drug & Cosmetic Act.

32. Novartis's allegations in the 2022 Citizen's Petition was that FDA could not permit removal of protected dosing information as doing so would result in a generic product with labeling that was "less safe" than ENTRESTO®. FDA summarily denied both of Novartis's petitions with fulsome responses on May 28, 2024 for the 2019 Citizen's Petition[25] and July 24, 2024 for the 2022 petition.[26]

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25 U.S. Food & Drug Admin., FDA-2019-P-1893-0010, Final Response Letter from FDA CDER to Novartis Pharmaceuticals Corporation (May 28, 2024), https://www.regulations.gov/document/FDA-2019-P-1893-0010.

26 U.S. Food & Drug Admin, FDA-2022-P-2228-0015, Final Response Letter from FDA CDER to Novartis Pharmaceuticals Corporation (Jul. 24, 2024), https://www.regulations.gov/document/FDA-2022-P-2228-0015.

33. After Novartis's failure to convince FDA to delay generic approvals failed via the submission of Citizen's Petitions, Novartis sued FDA on July 30, 2024 in the United States District Court for the District of Columbia claiming that FDA's approval of MSN's ANDA violated the Administrative Procedures Act (APA). In a Memorandum Opinion dated October 13, 2024, the United States District Court for the District of Columbia granted Summary Judgment in favor of FDA's finding that FDA did not violate the APA, the Federal Food Drug & Cosmetic Act, or FDA's implementing regulations. That case is now on appeal at the DC Circuit Court of Appeals, which recently denied Novartis's motion for an injunction pending appeal. Still undeterred, Novartis brought yet another suite in the USDC for the District of Columbia on January 13, 2025, CA No. 25-90. In this most recent suit, that to the best of my knowledge remains pending with the Court as of the date of this report, though the Court denied Novartis's request for emergency injunctive relief. Novartis again asks the Court to compel FDA to convert final approval of MSN's ANDA to tentative approval citing a pediatric exclusivity period that went into effect on January 15, 2025 upon expiration of US Patent No. 8,101,659. Novartis is leaving no stone unturned with respect to attempting to keep MSN's product from entering the market.

V. FDA GUIDANCE DOCUMENTS

34. FDA develops guidance documents to explain the agency's current position, interpretation, or policy in relation to a regulatory issue.[27] These guidance documents can address any number of practices, policies, expectations, procedures, or scientific matters related to the development, submission, review, approval and lifecycle maintenance of drug products.[28] All FDA guidance documents include a disclaimer that the recommendations contained within a guidance are not legally binding (with some limited exceptions).[29]

35. FDA publishes guidances to assist regulated industry with understanding FDA's views on how industry can most effectively reach their regulatory goals.[30] Generally speaking, sponsors that follow FDA's guidances when submitting their applications will experience a smoother review because the application sponsor is attempting to conform with FDA's most current position and interpretation of regulatory requirements.

36. Guidance documents are initially published as draft guidances with an associated comment period to permit industry to comment on the content of the

27 *Background: FDA Good Guidance Practices*, U.S. Food & Drug Admin., https://www.fda.gov/regulatory-information/guidances/background-fda-good-guidance-practices (last updated Dec. 17, 2024).

28 *Id.*

29 *Id.*

30 *Id.*

guidance or to ask additional clarifying questions for FDA to consider prior to issuance of a final guidance.[31] In some instances, FDA will follow an initial draft guidance with a draft Questions and Answers guidance to address questions received on the initial draft guidance.[32] This tactic is most frequently employed when FDA receives numerous comments on an initial draft guidance which may happen when FDA is changing its regulatory expectations for applicants. All FDA guidance are issued in accordance with FDA's Good Guidance Practice regulations at 21 CFR 10.115.[33]

VI. FDA GUIDANCE REGARDING THE APPEARANCE OF GENERIC DRUG TABLETS

37. To communicate expectations to the generic industry with respect to the physical characteristics of generic drug products, which would be substituted for their branded counterpart, FDA published Guidance for Industry titled "Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules" in June 2015 (Physical Attribute Guidance).[34]

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31 U.S. Food & Drug Admin, Draft Report and Plan on Best Practices for Guidance 5–6 (last visited Feb. 5, 2025), https://www.fda.gov/media/175121/download?attachment.

32 *See id.* at 21.

33 *See id.* at 5.

34 U.S. Food & Drug Admin., Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules: Guidance for Industry (June 2015), https://www.fda.gov/media/87344/download.

38. FDA stated that the purpose for issuance of this guidance was that the FDA was "concerned that differences in physical characteristics (e.g. size and shape of the tablet or capsule) may affect patient compliance and acceptability of medication regimens or could lead to medication errors. We believe these patient safety concerns are important, and we are recommending that generic drug manufacturers consider physical attributes when they develop quality target product profiles (QTPPs) for their generic product candidates."[35]

39. Thus, in order for a generic drug product to have a similar safety profile when compared to a branded Reference Listed Drug (RLD) the ANDA sponsor developing the generic must consider certain physical attributes including the size and shape of the generic product. FDA considers information from sponsors when the sponsor submits their ANDA to FDA for approval. FDA's Physical Attribute Guidance directs ANDA sponsors to submit information on the size of a tablet or capsule product in a specific section of an ANDA titled Description and Composition of the Drug Product of the ANDA, section 3.2.P.1 and states that FDA may request samples for evaluation of the physical attributes of the tablet or capsule.[36]

40. FDA's Physical Attribute Guidance includes a discussion of certain safety concerns related to swallowing oral tablets and capsules. Both the size and

35 *See id.* at 1.
36 *Id.* at 6.

shape of oral tablets and capsules impact a patient's ability to readily swallow these dosage forms while reducing difficulty or adverse events.[37] The Physical Attribute Guidance includes the following recommendation "For comparable ease of swallowing as well as patient acceptance and compliance with treatment regimens, the Agency recommends that generic oral tablets and capsules intended to be swallowed intact should be of similar size to the corresponding RLD."[38] FDA's Physical Attribute Guidance provides recommendations for differences in the largest dimension and the overall volume of the tablet or capsule.[39]

41. FDA's Physical Attribute Guidance also recognizes that the shape of a tablet or capsule is an important characteristic, noting that studies have shown that oval tablets may be easier to swallow and have faster esophageal transit times than round tablets of the same weight.[40] Patient compliance or adherence to their medication regimen may also be influenced by the size and shape of a tablet or capsule.[41]

42. Safety concerns related to the physical attributes of generic products have been studied by academics, where those findings generally suggest that patients

37 *Id.* at 2–6.
38 *Id.* at 4.
39 *Id.* at 5.
40 *Id.* at 5–6.
41 *Id.* at 3.

will have greater confidence in taking a generic product when it is similar in appearance to the branded RLD.[42]

43. ANDA sponsors that either ignore or choose not to follow FDA Guidance with respect to the Physical Attribute Guidance run the risk of receiving deficiencies from FDA ranging from comments issued in the context of an Information Request to a Complete Response Letter (CRL) refusing to approve the ANDA.[43] Because FDA considers Physical Attributes to correlate to the safety profile of a product, issuance of a CRL will often require the ANDA sponsor to reformulate their product to ensure that the safety profile of the generic product matches that of the branded RLD.

VII. COLOR CODING OF TABLETS SERVES AN IMPORTANT FUNCTION

44. In my experience, prudent developers of generic drugs know that compliance with FDA Guidance documents will often result in a smoother review of their ANDA with fewer questions from FDA. Alternatively, developers of generic drugs that do not comply with FDA Guidance will often experience protracted

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42 *See* Kesselheim, Aaraon S. et al., Variations in Pill Appearance of Antiepileptic Drugs and the Risk of Nonadherence, 173 JAMA Internal Medicine (2013).

43 U.S. Food & Drug Admin., Information Requests and Discipline Review Letters Under GDUFA: Guidance for Industry (Oct. 2022), https://www.fda.gov/media/109915/download; 21 C.F.R. 314.3 https://www.ecfr.gov/current/title-21/part-314/section-314.3#p-314.3(Complete%20response%20letter).

reviews with many questions and deficiencies that could have been easily avoided.[44] Because FDA has indicated that attributes such as size and shape should be considered as part of a QTPP analysis, generic developers will consider these attributes and endeavor to develop products that comply with FDA guidance including similarities with respect to size and shape.

45. Based upon my 22-year career in the Office of Generic Drugs, ANDA sponsors routinely consider using color schemes for their generic products that are similar to the branded RLD. Similarities in color scheme help ensure that patients are more readily able to further distinguish differences in products that have similar size and shape characteristics.[45]

46. This practice is evident with the ENTRESTO® products where the 24 mg/26 mg tablet and the 49 mg/51 mg tablet are both oval tablets with dimensions of 13.1 mm x 5.2 mm. With identical physical dimensions, a difference in color or

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44 *See* U.S. Food & Drug Admin., Good ANDA Submission Practices: Guidance for Industry at 29 (Jan. 2022), https://www.fda.gov/media/110689/download (describing various submissions that are required when the ANDA differs from product-specific guidelines).; Kurt R. Karst, "Size Matters," Says FDA, When it Comes to Generic Drug-RLD Sameness, FDA Law Blog (Jan. 4, 2012), https://www.thefdalawblog.com/2012/01/size-matters-says-fda-when-it-comes-to-generic-drug-rld-sameness/ (describing letters issued by OGDs to companies with pending ANDAs regarding tablet size differences).

45 *See* Kesselheim, supra note 42.

some other attribute (e.g. scoring or beveling) helps to ensure that patients are able to distinguish between different doses.

47. While ANDA sponsors are not required to employ the same color scheme as the RLD, there is a sound reason for ANDA sponsors to follow this practice as they are helping to ensure that patients are able to distinguish doses for similar products using the same functional cues as the color scheme of the branded RLD that a patient had been accustomed to receiving.

48. It doesn't take much imagination to realize the uncertainty that would arise if manufacturers of generic drugs simply chose to use a handful of tablet sizes and a single shape and color for all of their generic products. This would result in a world of patients taking either round or oval tablets, in two or three sizes from around 9 mm to 17 mm, which were all a single color where that color would likely be white. How could a patient being treated for heart failure, the primary indication of ENTRESTO®, with a generic of ENTRESTO® be able to distinguish their heart failure medication, from the medication they use to treat their kidney failure, their diabetes, their acid reflux, their seizures, and chronic arthritis. It is certainly not an uncommon occurrence for many patients to be treated with half a dozen or more oral medications to treat multiple disease states. Patients rely upon visual cues and other distinguishing factors such as color and shape to both identify the kind of medication they are taking and how many times a day they take that medication. These factors

are critical to ensure that patients are taking the right drug at the right time for the right condition.[46]

49. There are numerous examples of drug products where to visually distinguish different strengths of drug products for patients both the branded RLD and generic manufacturers utilize the same color scheme across the spectrum of strengths to enhance patient safety. Certain drug products with many strengths provide particularly useful examples.

50. One such product that remains in the marketplace is Synthroid® (levothyroxine) tablets, produced by AbbVie, Inc., which are available in 0.025 mg, 0.05 mg, 0.075 mg, 0.88 mg, 0.1 mg, 0.112 mg, 0.125 mg, 0.137 mg, 0.15 mg, 0.175 mg, 0.2 mg and 0.3 mg. Synthroid's tablets are all round tablets with the following colors: 0.025 mg is orange, 0.050 mg is white, 0.075 mg is purple, 0.88 mg is green, 0.1 mg is yellow, 0.112 mg is red, 0.125 mg is brown, 0.137 mg is blue(turquoise), 0.15 mg is blue, 0.175 mg is purple(lilac), 0.2 mg is pink, and 0.3 mg is green.[47]

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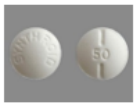
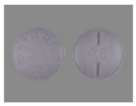
46 Greene JA, Kesselheim AS. Why do the same drugs look different? Pills, trade dress, and public health. N Engl J Med. 2011 Jul 7;365(1):83-9. doi: 10.1056/NEJMhle1101722. PMID: 21732842.

47 Label for Synthroid, AbbVie, Inc. *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=1e11ad30-1041-4520-10b0-8f9d30d30fcc (last visited Feb. 5, 2025). Images for all charts are from Drugs.com. *See* Declaration of Jacquellena T. Carrero ("Carrero Decl."), Ex. 3.

Synthroid® (levothyroxine) AbbVie | NDA 21402					
					
0.025 mg	0.05 mg	0.075 mg	0.088 mg	0.1 mg	0.112mg
					
0.125 mg	0.137 mg	0.15 mg	0.175 mg	0.2 mg	0.3 mg

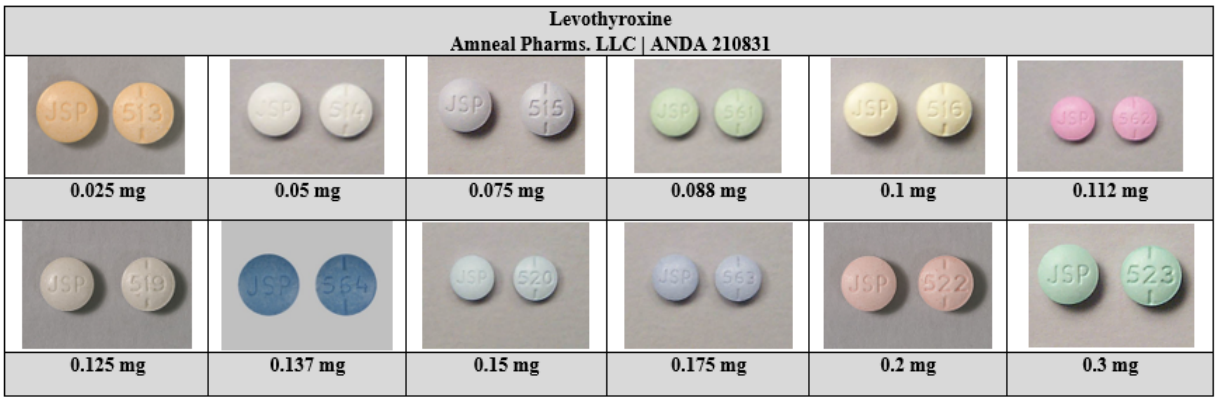
51. Consistent with the practice and guidance discussed above, several entities who have filed ANDA's for this product follow the same color-coding scheme:

a. ANDA 212399 from Accord Healthcare, Inc. is available as a 7 mm round tablet employing the same color scheme,[48]

Levothyroxine Accord Healthcare Inc. | ANDA 212399					
					
0.025 mg	0.05 mg	0.075 mg	0.088 mg	0.1 mg	0.112 mg
					
0.125 mg	0.137 mg	0.15 mg	0.175 mg	0.2 mg	0.3 mg

48 Label for Levothyroxine Sodium, Accord Healthcare, Inc.. *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a6233381-3043-4e9a-aaa6-a6b105e5142b (last visited Feb. 5, 2025).

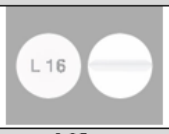
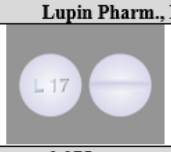
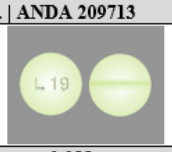
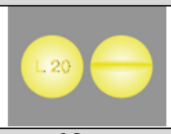
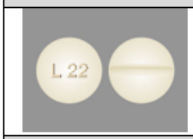
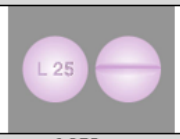
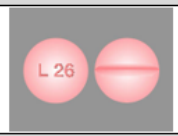
b. ANDA 210831 from Amneal Pharmaceuticals LLC is available as a 9 mm round tablets employing the same color scheme with exception of its 0.112 mg which is described as dark pink,[49]



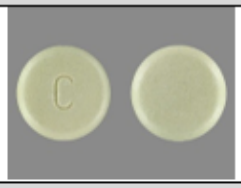
c. ANDA 209713 from Lupin Pharmaceuticals, Inc. is available as a 6 mm round tablet employing the same color scheme with exception of its 0.112 mg which is described as pink.[50]

49 Label for Levothyroxine Sodium, Amneal Pharmaceuticals NY LLC. *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b0efcd19-42a3-4ddb-af5a-16cd073a492a (last visited Feb. 5, 2025).

50 Label for Levothyroxine Sodium, Lupin Pharmaceuticals, Inc.. *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=18717e58-89fb-4e2f-93b6-d6ac3e988d37 (last visited Feb. 5, 2025).

Levothyroxine Lupin Pharm., Inc. | ANDA 209713					
					
0.025 mg	0.05 mg	0.075 mg	0.088 mg	0.1 mg	0.112 mg
					
0.125 mg	0.137 mg	0.15 mg	0.175 mg	0.2 mg	0.3 mg

52. Novartis's own products also aren't immune from having ANDA sponsors employ the same physical attributes as Novartis's branded RLD. One such Novartis example is their product marketed under the proprietary name Myfortic® (mycophenolic sodium) Delayed-release Tablets NDA 50791. Novartis' most recently updated labeling and drug listing information available on DailyMed describes Myfortic® Delayed-release Tablets, 180 mg as 10 mm, round, green, tablets and 360 mg as 18 mm, oval (ovaloid), orange, tablets.[51]

Myfortic® (mycophenolic sodium) Delayed-Release Tablets Novartis Pharm. Corp. | NDA 50791	
	
180 mg	360 mg

51 Label for Myfortic, Novartis Pharms. Corp., *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=eed26501-890d-4ff6-88e7-6dbea4726e53 (last visited Feb. 5, 2025).

53. Like the other examples noted above, filers of ANDA reference these color combinations in keeping with the FDA guidance:

a. ANDA 216637 from Novugen Pharma (USA) LLC is available in 180 mg as 10 mm, round, green tablets and 360 mg as 18 mm, oval (ovaloid), orange, tablets.[52]

b. ANDA 214376 from Slate Run Pharmaceuticals LLC is available as 10 mm, round, green, tablets, and 360 mg as 17 mm, oval, orange, tablets.[53]

c. ANDA 202555 from Accord Healthcare Inc. is available in 180 mg as 10 mm round, green tablets and 360 mg as 17 mm, oval(oblong), orange tablets.[54]

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52 Label for Mycophenolic Acid Tablet, Delayed Release, Novugen Pharma (USA) LLC, *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=cbc3e916-09e2-4e6e-9e5e-98375f5e6d41 (last visited Feb. 5, 2025).

53 Label for Mycophenolic Acid Tablet, Delayed Release, Slate Run Pharmaceuticals LLC, *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=c1ce92ef-4102-1487-e053-2995a90ac521 (last visited Feb. 5, 2025).

54 Label for Mycophenolic Acid Tablet, Delayed Release, Accord Healthcare Inc., *available at* DailyMed, Nat. Inst. of Health, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=dc24aa15-330c-4698-872f-159d7e582b4b (last visited Feb. 5, 2025).

Mycophenolic sodium Accord Healthcare Inc. | ANDA 202555	
	
180 mg	360 mg

54. Other ANDAs for Entresto also follow the size and color dosing regimes.

55. I understand that at least 17 other companies have also filed ANDAs to release a generic version of Entresto and as of February 5, 2025, FDA had approved 11 ANDAs from different ANDA sponsors.[55]

56. Consistent the practices noted above, the publicly available information regarding these ANDAs show that they also follow the color schemes and sizes of Novartis' Entresto product:[56]

Sacubitril and Valsartan Tablets – Innovator and Generics comparison						
Parameters	**ENTRESTO (NOVARTIS PHARMS CORP)**	**MSN Laboratories Private Limited (Novadoz Pharmaceuticals LLC)**	**Torrent Pharmaceuticals Limited**	**Laurus Labs Limited**	**Ascend Laboratories, LLC**	**Alembic Pharmaceuticals Inc.**

55 *See* U.S. Food & Drug Admin., Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm (last visited Feb. 5, 2025) (database listing approved ANDAs for sacubitril and valsartan tablets).

56 For sources of information contained in this chart, see Carrero Decl. Exs. 7–12.

NDA/ ANDA #	**NDA 207620**	**ANDA 213748**	**ANDA 213604**	**ANDA 213676**	**ANDA 213674**	**ANDA 213682**
Description						
24 mg/ 26 mg	Violet white unscored, ovaloid, biconvex, film-coated tablets debossed with "NVR" on one side and "LZ" on the other side.	Purple colored, oval shaped, biconvex, film coated tablets one side debossed with "M" and other side debossed with "S1"	Violet white colored, round shaped, biconvex, film coated tablet with beveled edges, unscored, debossed with "U4" on one side and plain on the other side.	Violet white color, oval shaped, biconvex film-coated tablets debossed with "S5" on one side and plain on the other side	Off white to light pink unscored, ovaloid, biconvex, film-coated tablets, "SV5" on one side and plain on the other side	white to off white, modified capsule shaped, biconvex film-coated tablets debossed with "725" on one side and "L" on the other side.
49 mg / 51 mg	Pale yellow unscored, ovaloid, biconvex, film-coated tablets debossed with "NVR" on one side and "L1" on the other side.	Light yellow to yellow colored, oval shaped, biconvex, film coated tablets one side debossed with "M" and other side debossed with "S2"	Pale yellow colored, oval shaped, biconvex, film coated tablet with beveled edges, unscored, debossed with "U5" on one side and plain on other side.	Pale yellow color, oval shaped, biconvex film-coated tablets debossed with "S1" on one side and plain on the other side.	Pale yellow to yellow unscored, ovaloid, biconvex, film-coated tablets, "SV1" on one side and plain on the other side	light yellow to yellow, modified capsule shaped, biconvex film-coated tablets debossed with "726" on one side and "L" on the other side.
97 mg/ 103 mg	Light pink unscored, ovaloid, biconvex, film-coated tablets debossed with "NVR" on one side and "L11" on the other side	Light pink to pink colored, oval shaped, biconvex, film coated tablets one side debossed with "M" and other side debossed with "S3"	Light pink colored, oval shaped, biconvex, film coated tablet with beveled edges, unscored, debossed with "U7" on one side and plain on other side.	Light pink color, oval shaped, biconvex film-coated tablets debossed with "S2" on one side and plain on the other side.	Light pink to pink unscored, ovaloid, biconvex, film-coated tablets, "SV2" on one side and plain on the other side	light pink to pink, modified capsule shaped, biconvex film-coated tablets debossed with "L727" on one side and plain on the other side.
Dimen-sions (Roun-ded)						
24 mg/ 26 mg	13 mm	10 mm	6 mm	9 mm	10 mm	9 mm

49 mg / 51 mg	13 mm	13 mm	11 mm	12 mm	13 mm	12 mm
97 mg/ 103 mg	15 mm	15 mm	15 mm	15 mm	15 mm	15 mm
Shape	OVAL (ovaloid biconvex)	OVAL	24 mg/26 mg – ROUND 49 mg / 51 mg and 97 mg/ 103 mg - OVAL (biconvex tablet with beveled edges)	OVAL (biconvex)	OVAL (Ovaloid biconvex)	CAPSULE (biconvex)
DailyMed Link	https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=000dc81d-ab91-450c-8eae-8eb74e72296f	https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=44db8114-622e-41f6-96a1-447d47b0267c	https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=59b7a07a-96ee-44b1-8dae-2b42169aa2c5	https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b47b5c7e-1c20-429c-9560-07f5f06cdce3	https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=98d838f6-03a9-43e9-b8dd-8882c6df1631	https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5928f174-83e5-4c74-b15a-138338a70295
Exhibit with DailyMed Web-pages and Drug Label Infor-mation	Carrero Decl. Ex. 7	Carrero Decl. Ex. 8	Carrero Decl. Ex. 9	Carrero Decl. Ex. 10	Carrero Decl. Ex. 11	Carrero Decl. Ex. 12

57. It is readily apparent from these examples that ANDA which follow the physical attributes, including color, of a branded RLD are routinely reviewed and approved by FDA and are available in the marketplace.

VIII. IRREPARABLE HARM TO MSN

58. I understand that Novartis has asked the Court for a preliminary injunction enjoining and restraining Defendants from distributing a generic sacubitril/valsartan drug.

59. The effect of such an order would mean that MSN could not launch its product and all its investment in research and development over years would be placed at risk.

60. First, there is no way to simply change the size, shape, and color of the tablet without essentially starting over with the entire process at the FDA for regulatory approval. Reformulation of a developed product to change the physical attributes of the product amounts to an ANDA sponsor needing to completely restart development of a specific product.[57] FDA Guidance on this matter clearly states that changes in color, size, or shape would need to be submitted as a Prior Approval Supplement (PAS) to an approved ANDA.[58] Such a PAS would need to include new exhibit batches, and a minimum of 6 months of stability under accelerated conditions (40 degrees Centigrade/ 75% relative humidity) and ambient conditions(25 C/60% RH). Notably, prior to manufacturing exhibit batches, MSN would need to develop the new product to determine what size and shape is feasible and whether transition to a new size and shape required any alterations to the formulation of the product, this development work would precede exhibit batch manufacturing. It is also highly likely that the Office of Generic Drugs would require

57 *SUPAC-IR Questions and Answers about SUPAC-IR Guidance*, U.S. Food & Drug Admin. (Feb. 18, 1997), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/supac-ir-questions-and-answers-about-supac-ir-guidance.

58 *Id.*

the ANDA sponsor to complete a new fasting bioequivalence study comparing the new proposed product to the branded RLD. FDA's review of the PAS would be governed by the Generic Drug User Fee Act III Commitment Letter. Because there are already 11 ANDAs that have been approved by FDA for generic versions of ENTRESTO®, a hypothetical PAS submitted by MSN would not be eligible for priority review, with the resulting review from FDA being completed in either 6 months or 10 months. The 6-month timeframe would apply if there was no facility referenced in the PAS that required FDA inspection and the 10-month review would apply if any inspection was needed.

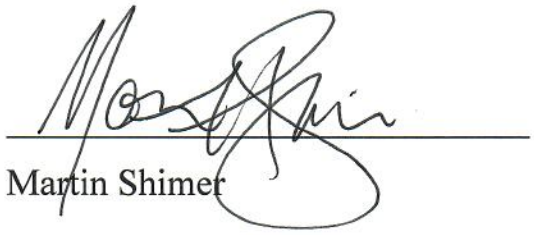
61. Second, in my experience, any delay in bringing a generic to market would have devasting consequences as it would place the generic sponsor at a competitive disadvantage with other generics able to launch. Generally speaking, the first ANDA applicant that is able to enter into the highly competitive generic marketplace is at a distinct advantage over other ANDA applicants that enter the market at a later date. This concept is generally referred to as the first-mover advantage. The first sponsor to enter the market is generally able to enter into purchasing contracts in advance of competitors and as previously stated in paragraph 19, the first sponsor to enter the generic marketplace is usually able to sell their product at a higher price for a period of time until other competitors are able to enter the market.

62. In essence, Novartis asks this Court to effectively overturn an approval decision for a drug product that FDA has reviewed and approved thus determining that MSN's product is an equivalent of and provides a similar safety profile to ENTRESTO®.

63. Novartis thus asks this Court to return MSN to development of their product with the goal of developing a product that is less similar to ENTRESTO® and may in FDA's view, per concepts communicated by FDA in the Physical Attribute Guidance, result in a product that is less safe or more confusing for patients.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Dated: February 6, 2025



Martin Shimer